Haemorrhagic Septicaemia

M.C.L. De Alwis

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Preface

The first monograph on haemorrhagic septicaemia (HS) was published by the Food and Agriculture Organization (FAO) in 1962. Two decades later, following a recommendation of the Third International Workshop on Haemorrhagic Septicaemia (December 1979), this monograph was revised and updated and a new edition was published in 1982. During the 1980s and 1990s, there has been a considerable amount of research on HS and a vast amount of new information has become available. A significant feature of this period was the collaborative work by Australian scientists with scientists in many Asian countries, supported by the Australian Centre for International Agricultural Research (ACIAR). This has led to the introduction of new technologies into haemorrhagic septicaemia research and development. The FAO has also funded a number of projects on HS in the Asian region.

This monograph attempts to capture all the new information generated through these projects — to enrich and add to the available information and present it in a form that will address the needs of a wide readership. It seeks to satisfy multiple roles, including that of a textbook, a review and a laboratory manual. It is, therefore, targeted for veterinary students, practising veterinarians, research workers and also animal health administrators and policy makers.

I have endeavoured to incorporate into this monograph all accessible published and unpublished information, as well as my own experiences with the disease. The information on enzyme-linked immunosorbent assay (ELISA) and molecular techniques (Appendixes 3–6) was kindly contributed by Dr Kirsty Townsend of the School of Veterinary Science and Animal Production, The University of Queensland. The photographs were contributed by Dr Neil Horadagoda of the Faculty of Veterinary Medicine and Animal Science, University of Peradeniya, and the staff of the Veterinary Research Institute, Peradeniya, Sri Lanka (the FAO Regional Reference Centre for Haemorrhagic Septicaemia). These contributions, and the interest and support of ACIAR, are gratefully acknowledged.

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Introduction

Haemorrhagic septicaemia (HS) is an acute, fatal, septicaemic disease of cattle and buffaloes caused by specific serotypes of the bacterium *Pasteurella multocida*. The numerous serotypes of *P. multocida* are associated with a variety of disease syndromes in a wide range of agricultural, domestic and feral animal species. In many instances *pasteurella* plays a secondary role in the pathogenesis of the disease or acts in combination with other agents. HS, on the other hand, is a primary pasteurellosis and is reproducible in susceptible host species using pure cultures of the causative organism alone. This is comparable to typhoid fever, for example, which is a specific form of salmonellosis caused by a specific strain of salmonella in a specific host species.

HS can be controlled by vaccination and most countries where the disease is endemic resort to routine prophylactic vaccination. The vaccines currently in routine use are satisfactory and strategic vaccination programs have resulted in substantial reduction in the losses. However, research is in progress for the development of an improved vaccine, to overcome some remaining weaknesses in the current vaccines.

HS occurs most commonly in cattle and buffaloes. Buffaloes are more susceptible than cattle and the disease occurs more frequently in poor husbandry conditions. Clinical symptoms are often not observed but include high temperature, loss of appetite, nasal discharge, increased salivation and laboured breathing, with swellings in the submandibular region. Death usually occurs quickly and mortality is virtually 100% in infected animals. True recovery from clinical disease occurs only if the animal is treated in the very early stages, which is often impossible under prevailing field conditions.

HS has been recorded in almost all parts of the world except for Oceania, including Australia, where it has never occurred. Its distribution is related to climatic conditions, husbandry practices and the types of animals reared. The disease is of great economic importance in Asia where cattle and buffaloes are abundant and are vital for draught power and milk production. It is less important in Africa where there are relatively few cattle and buffaloes and because other animal diseases cause relatively more severe economic losses.

Although the conventional host species are cattle and buffaloes, *P. multocida* has been reported or suspected in Bali cattle, pigs, goats, sheep, horses, donkeys, African buffaloes, camels, yaks and poultry.

Explosive outbreaks of HS may occur when it is first introduced to areas that have previously been free of the disease, or when it occurs as sporadic outbreaks in nonendemic areas. In endemic areas, large numbers of animals that survive after an outbreak of disease become latent carriers. They intermittently shed the organisms but, since the herd immunity is also high, there are no fresh clinical cases. A new outbreak occurs when a shedder comes into contact with a susceptible animal, which may be one born after the previous outbreak or one introduced into the herd from elsewhere. The chance of a fresh outbreak increases with time with an increase in size of the susceptible population.

Movement of animals can precipitate new outbreaks of disease in two ways. Firstly, the animals moved may be carriers and may infect susceptible stock. Secondly, the animals moved may be susceptible to the disease and become infected from native immune carriers. In either case, explosive outbreaks can result.

Once the first clinical case occurs, more bacteria are shed and disseminated. Their survival in the environment and transmission to other animals depend on factors such as closeness of contact, hygiene and climate (wet conditions prolong the survival of the causative bacteria outside the animal, making an outbreak more likely). The size of the outbreak depends on the proportion of immune to nonimmune animals in the herd. Occasional sporadic outbreaks allow the build up of nonimmune animals and a major outbreak may occur. Regular seasonal outbreaks result in much higher herd immunity (through frequent exposure) and outbreaks that do occur therefore tend to be less significant.

Several international organisations have played a significant role in assisting in the control of HS. These are the Food and Agriculture Organization (FAO) of the United Nations, the Office International des Epizooties (OIE, a world organisation for animal health) and the Australian Centre for International Agricultural Research (ACIAR). The assistance provided by these organisations includes encouragement and funding of
research, development of diagnostic techniques and vaccine production technologies and facilitating control of the disease through strengthening and establishment of diagnostic and vaccine production facilities in the countries where the disease exists.

Outline of monograph

In this monograph an attempt has been made to bring together all the current information on HS. This includes the global distribution and economic importance of the disease (Chapter 1); a review of the causative organism (Pasteurella) and its relationship to HS and other animal diseases of economic importance (Chapter 2); and the mode of infection, clinical signs and pathology (Chapter 3), epidemiology (Chapter 4), diagnosis (Chapter 5), and treatment and control (Chapter 6) of HS. Chapters 7, 8 and 9 are devoted to the types of vaccines currently available, vaccination programs and vaccine research and development, respectively. Some priority areas for future research are identified in Chapter 10.

The appendixes give details of laboratory techniques for diagnosis and technologies for production and quality control of vaccines. These include simplified methods that can be carried out in any modestly equipped laboratory in the developing countries where the disease is endemic, and sophisticated molecular techniques that are mainly research tools at present but may, in time, emerge as routine procedures.
Global Distribution and Economic Importance

Overview

Global distribution
Haemorrhagic septicaemia (HS) has a wide global distribution. In most Asian and African countries, it is endemic. Other countries have recorded a low sporadic or exceptional occurrence. In a few other countries the disease has been suspected clinically but has not been confirmed by serology. HS has never been reported in a few countries, including the United Kingdom, Oceania (including Australia) and some European countries.

Economic importance
Most Asian countries rank HS as one of the most economically important diseases or the most economically important bacterial disease. The Office International des Epizooties (OIE) classifies HS with a number of other bacterial and parasitic diseases as a List B disease.

1.1 Global Distribution

Haemorrhagic septicaemia (HS) has been recorded in almost all parts of the world except for Oceania, including Australia, where it has never occurred (see Table 1.1).

It occurs in South and Southeast Asia, including Indonesia, the Philippines, Thailand and Malaysia. The disease was first reported as early as the 1880s in Malaysia (FAO 1991). In Sri Lanka, it was first reported in 1911 but assumed epidemic proportions in the mid-1950s and routine vaccination was introduced in 1957. It is believed to have been introduced into the Philippines in buffaloes (carabaos) imported from Hong Kong in 1902 and in a shipment of cattle imported from Shanghai in 1903. However, the first authentic reports of the disease in the Philippines were from the Visayas and in Bulacan, Luzon. After this, sporadic cases were reported until the mid-1950s when the disease had spread to 40 of the 54 provinces (FAO 1959).

HS has been reported in the Near and Middle East, southern Europe and North, Central and East Africa. There are records of HS in Iran dating back to the 1930s, and a serious study of the disease was made at the Razi Institute in 1935. A saponin adjuvanted vaccine has been used as an immunising agent in Iran since 1938 (FAO 1959). There is a report of HS occurrence in South Africa (Bastianello and Jonker 1981).

In the United States, the disease was reported among bison in national parks in 1912, 1922 and 1965–67. Outbreaks were also reported among dairy cattle in New Jersey in 1969 and among beef calves in California in 1993 (Heddleston et al. 1967; Carter 1982; Blanchard et al. 1993). In summer 1993, an outbreak was reported among beef calves in New Brunswick, Canada (Rimler and Wilson 1994). Cultures from these outbreaks are still available in collections and confirm the diagnosis. However, apart from these
sporadic outbreaks, the disease has not become endemic in North America.

HS was recognised in Japan as early as 1923 but has not been recorded since 1954 and was never endemic (Carter 1984; FAO 1959).

The disease has never been reported in Oceania (including Australia), or most of western Europe. There have been some reports suggestive of HS from some Central and South American states, and from southern and eastern European countries (FAO–WHO–OIE Animal Health Yearbook 1994) but these reports are not supported by serotype identification for confirmation. Table 1.1 gives a summary of the global distribution of the disease. It is likely that HS may occur in some South American countries with high water buffalo populations, and where conditions are somewhat similar to those prevailing in tropical Asia.

1.2 Economic Importance

1.2.1 Asia

Asia has 423 million cattle and 145 million buffaloes — 33% and 95%, respectively, of the world’s populations of these species.

Cattle and buffaloes are reared mainly for use as draught animals in the rice fields, but in India and, to a lesser extent, Pakistan, milk production is also important (FAO 1994, 1995). In Asia as a whole, buffaloes contribute 37% of milk production but in India, where the production of milk is the highest in Asia, nearly 50% of the milk is produced from buffaloes.

Where animals are used for draught power, which is a seasonal activity, they are managed in an extensive, free-range system for most of the year. Such conditions are an ideal environment for the spread of diseases such as HS because herds of animals belonging to different owners roam together in common grasslands, drink in common village tanks and are often even paddocked together at night. Such animals are often less well managed, with lower vaccination coverage, than more intensively farmed animals.

The relatively high buffalo population in Asia, together with the higher susceptibility of this species to the disease and the high case fatality (see Chapter 4), all highlight the significance of the economic losses caused by HS in the Asian region.

Diseases such as rinderpest have now been effectively controlled or eradicated, while foot-and-mouth disease (FMD) has a low mortality (particularly among animals indigenous to the region). Hence, HS has emerged as a disease of considerable economic importance in the Asian region.

1.2.2 Africa

HS is of less economic importance in the African region than in Asia. This is because Africa has less of the world’s cattle and buffalo populations, with only 15% and 2% for cattle and buffaloes, respectively (FAO 1995). Also, many other animal diseases cause more severe economic losses. These include the African endemic diseases, such as trypanosomiasis (nagana), theileriosis (East Coast fever) and contagious bovine pleuropneumonia; and also rinderpest and FMD, which are common to both Africa and Asia. Published reports on economic losses in the African region are scarce.

1.3 Economic Losses in Asia

The actual economic losses due to HS are difficult to determine. The prevalence of HS and the morbidity and mortality rates are known in most Asian countries and a few countries have attempted to quantify the losses. However, since the methods used have varied from one country to another, the findings are not strictly comparable.

The problem is that many factors need to be considered in computing economic losses. For example, HS occurs mainly in situations where husbandry practices are poor and animals are reared under a free-range system. In such situations, disease-reporting systems, particularly passive systems that depend on the owner or farmer notifying the relevant authorities, are poorly developed. Thus, a wide discrepancy is
Table 1.1. Summary of the global distribution of haemorrhagic septicaemia.

<table>
<thead>
<tr>
<th>Disease endemic</th>
<th>Low sporadic or exceptional occurrence</th>
<th>Suspected but not confirmed</th>
<th>Probably existed Now free&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Never occurred</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASIA</td>
<td>Malaysia (Sabah)</td>
<td>Kuwait, Qatar</td>
<td>Hong Kong (1984), Israel (1948), Singapore (1930)</td>
<td>Cyprus, Japan, Jordan</td>
</tr>
<tr>
<td></td>
<td>Bhutan, China, India, Indonesia, Malaysia, Mongolia, Myanmar, Philippines, Sri Lanka</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Central African Republic, Chad, Ivory Coast, Ghana, Guinea, Kenya, Mozambique, Niger, Nigeria, South Africa, Zimbabwe</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AMERICA</td>
<td>Canada, Jamaica, United States</td>
<td>Antigua and Baruda, El Salvador (1990), Paraguay (1985), St Kitts and Nevis</td>
<td>Barbados, Belize, Bolivia, Chile, Cuba, Haiti, Mexico</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Argentine, Brazil (part), Ecuador, Falkland Islands, Honduras, Nicaragua, Venezuela</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EUROPE</td>
<td>Estonia, Latvia, Portugal, Russian Federation, Spain</td>
<td>Albania, Austria, Croatia, Greece</td>
<td>Finland (1993), Germany (1986), Iceland, Italy, Luxembourg, Macedonia, Malta, Poland (1985), Romania (1993), Sweden, Switzerland, Isle of Man, Yugoslavia</td>
<td>Czech Republic, Denmark, France, Iceland, Lithuania, Maldova, Slovenia, United Kingdom</td>
</tr>
<tr>
<td>OCEANIA</td>
<td></td>
<td></td>
<td></td>
<td>Australia, New Caledonia, New Zealand, Vanuatu</td>
</tr>
</tbody>
</table>

<sup>a</sup> The year indicated within brackets is the known year of last occurrence. In other instances, year of last occurrence is unknown.

Source: FAO-OIE-WHO Animal Health Yearbook 1994. Only countries which submitted information on haemorrhagic septicaemia for the year are included.
bound to exist between actual deaths and reported deaths. This is borne out by the findings of an active surveillance study carried out in Sri Lanka (De Alwis and Vipulasiri 1980) compared to the reported deaths in that country (see Section 1.3.1).

Secondly, losses cannot merely be restricted to the market value of the animal at the time of death. The productive potential of the animal, its reproductive capacity and, in the case of draught power loss, the cost of alternate sources of draught power have to be taken into account. Singh et al. (1987) in India and Ahmed (1996) in Bangladesh attempted to quantify these losses. The Indian study was location-specific, restricted to one village and covered all animal diseases including HS. The Bangladesh study covered several selected diseases in the entire country.

A summary of the economic studies that have been reported in South and Southeast Asian countries is given below. However, all the available information indicates that the actual losses are considerably higher than the values calculated in the studies.

1.3.1 South Asia

India has a sizeable cattle and buffalo population of 192 million and 70 million, respectively. From 1936 to 1944, there were an average of 700 reported outbreaks of HS and 40 000 deaths per year. During the 1950s, the average reported deaths per year ranged from 30 000 to 60 000. In the 1960s and 1970s this figure dropped to approximately 4000 per year, presumably due to improved control measures (FAO 1991).

Dutta et al. (1990) estimated that in India during the past four decades HS has accounted for 46–55% of all bovine deaths. They also reported that from 1974 to 1986, HS accounted for 6.3 deaths per year for every 100 000 bovine population. This amounted to 58.8% of the aggregate of bovine deaths due to the five epidemic diseases FMD, rinderpest, black quarter, anthrax and HS. Before 1939, the corresponding figure ranged from 13.4 to 20.9%. Thus, it appears that HS has increased in economic importance in relation to the other four epidemic diseases.

In a location-specific study in India, Singh et al. (1987) computed all of the losses from mortality and productivity, as well as reproductive losses and losses incurred in disease control programs, and concluded that FMD, HS and gastrointestinal parasitism were the most economically important diseases of cattle.

Pakistan ranks HS as a disease of considerable economic importance, with 34.1% of all deaths in susceptible animals caused by HS (FAO 1979). Pakistan has a cattle population of 17.7 million, and a buffalo population of 18.8 million, the latter being proportionately higher than most other countries in the region. In 1978, annual economic losses from HS were estimated at 1.89 billion Pakistan rupees (PKR) or US$189 million (Chaudhry and Khan 1978; Sheikh et al. 1994). In a study conducted in 10 of the 95 villages in the district of Lahore, Khan et al. (1994) found HS, FMD and gastrointestinal diseases to be the main causes of economic losses. The annual financial loss due to disease was estimated as PKR 19 million, of which PKR 6.8 million was attributed to HS.

Nepal, with 6.3 million cattle and 3.0 million buffalo, ranked HS as the second most important infectious disease after rinderpest and the most important bacterial disease. In a retrospective study of veterinary hospital records maintained in four districts of Nepal during 1985–90, Thakuri et al. (1992) found that parasitic diseases and infectious diseases accounted for 54% and 24% of all cases, respectively, and HS was the most frequent infectious disease.

In 1978 the Food and Agriculture Organization and United Nations Development Program coordinated a survey on the impact of disease on production in the Azad State of Jammu and Kashmir, near the border of India and Pakistan. The survey was carried out as part of the National Program for Livestock and Dairy Development. It showed that nutritional disorders and parasitism were the greatest sources of loss in livestock. Of the bacterial diseases, however, HS and black quarter made the most significant contribution to losses.

In Sri Lanka, an island of 65 000 km², HS first assumed epidemic proportions in 1955–56, with around 5000 reported deaths from a cattle and buffalo population of around 2.5 million. Thereafter, through various control measures, the losses were reduced to about 1200
reported deaths per year in the early 1980s and had declined further to 269 in 1990 (FAO 1991). These reports were derived from a passive reporting system. Of the 24 administrative districts in the country, the disease is endemic in all of 13 districts and parts of four other districts, covering around two-thirds of the total land area. There has been an active surveillance study in six selected locations within the endemic zone (De Alwis and Vipulasiri 1980) covering 22 297 buffaloes in 803 herds and 20 878 cattle in 870 herds. This study has indicated that 15.2% of buffaloes and 8.1% of cattle die of HS each year. When these findings were extrapolated to the entire endemic zone, considering the carcase value alone, a modest estimate of economic loss was 90 million Sri Lankan rupees (SLR), equivalent to US$6 million at that time.

Bangladesh has 23.4 million cattle and 0.8 million buffaloes. When only the production of milk, meat and eggs was considered, the contribution of the livestock sector to the economy was calculated to be about 9%. When the value of draught power, rural transport and the use of dung as fertiliser and domestic fuel were also computed, it was reported to be around 15%. Of the bacterial diseases of cattle and buffaloes present in Bangladesh, black quarter was ranked as the most important, with anthrax and HS equal second in economic importance (Ahmed 1996).

Ahmed (1996) also estimated that of a total economic loss of US$148.6 million each year due to these three diseases, direct losses account for only US$2.3 million. Direct losses include the market value of animals that died and the cost of treatment for those that recovered. Indirect losses in this computation took into account the value of the rice that would have been produced from the land left uncultivated as a result of lack of draught power.

However, it did not include potential productive (milk and meat) and reproductive capacities of the animals. It is also noteworthy that this study used retrospective computerised data, which were probably the product of a passive, routine reporting system. The difference between losses computed from such an information system and an active surveillance study was very evident in a project carried out in Sri Lanka (De Alwis and Vipulasiri 1980).

1.3.2 Southeast Asia

Indonesia has 9.5 million cattle and nearly 3.3 million buffaloes, of which around 97% are used for draught power. The livestock sector contributes around 10% to total agricultural output (ACIAR 1993: Country Reports). Estimates of economic losses due to HS have ranged from US$3500 to US$6000 (FAO 1991; ACIAR 1993: Country Reports). In a study of diseases affecting animals used for draught power in Indonesia (Partoutomo et al. 1985), which included large ruminants and horses, HS was ranked fourth, after fascioliasis, trypanosomiasis and FMD.

Malaysia has a relatively small population of 735 000 cattle and 186 000 buffaloes (FAO 1994). In the early years, an average of 28.7 outbreaks per year were reported, with an average mortality of 12.6% per outbreak (FAO 1979). During 1967–76, 287 outbreaks were recorded in peninsular Malaysia with 3605 deaths (FAO 1991). During 1980–89, the losses due to HS were estimated as 2.25 million Malaysian ringgit (US$0.85 million).

The Philippines has 1.67 million cattle and 2.65 million buffaloes (ACIAR 1993). In 1990, the Philippines reported 14 331 cases of HS in cattle, with 1057 deaths; and 17 720 cases in buffaloes, with 1725 deaths.

Myanmar lists FMD, HS, black quarter and anthrax as the four most important diseases that cause economic losses in its 11.5 million cattle and buffaloes (of which 6.3 million are used for draught). It has been estimated that 50% of the government’s effort in disease control is for the control of HS. Through regular, high vaccination coverage, the disease has been effectively controlled in middle and lower Myanmar. In the northern and eastern regions, however, the disease remains endemic and 20–30 outbreaks are reported each year, with around 1000 deaths (ACIAR 1993).

Thailand has 5.5 million cattle and 4.7 million buffaloes, spread over 513 115 km$^2$. Only 35 outbreaks of HS have been reported, with 3.64 deaths per outbreak. It is believed that losses may have been unreported (FAO 1991; ACIAR 1993).

Vietnam, the Lao People’s Democratic Republic (Laos) and Cambodia rank HS as one of the most
economically important diseases. In Laos, however, the number of reported deaths has dropped from 16,000 in 1981 to 7,500 in 1990. The economic losses from HS were estimated at US$1.4 million in 1990 (FAO 1991, ACIAR 1993).

1.4 The Role of International Organisations

Several international organisations have played a significant role assisting in the control of HS. These are the Food and Agriculture Organization (FAO) of the United Nations, the Office International des Epizooties (OIE) and the Australian Centre for International Agricultural Research (ACIAR). The assistance provided by these organisations includes encouragement and funding of research, development of diagnostic techniques and vaccine production technologies and facilitating control of the disease through strengthening and establishment of diagnostic and vaccine production facilities in the countries where the disease exists.

1.4.1 Office International des Epizooties

The OIE, or World Organisation for Animal Health, was established in 1924. The main activities of the organisation are:

- to collect and disseminate to its member countries information on the occurrence, course and treatment of animal diseases;
- to provide guidelines and standards of health regulations applicable to international trade in animals; and
- to promote and coordinate research on pathology, diagnosis, treatment and prevention of animal diseases when international collaboration in such research is desirable.

For the purpose of the above activities animal diseases are classified into two categories, Lists A and B. List A consists of those diseases that spread rapidly, and the scope of which extends beyond national borders. These diseases have particularly serious socioeconomic or public health consequences and are of major importance in the international trade of animals and animal products.

List B includes diseases that are also considered to be of socioeconomic and/or public health importance within countries, and which are also of significance to the international trade in animals and animal products. HS is included in List B. This classification largely influences the priority status given to livestock diseases by respective governments in endemic countries in their allocation of resources for disease control.

The OIE does not have any regional programs for the control/eradication of HS as for rinderpest and FMD. These two latter diseases are in List A (see above). Where necessary, however, there are opportunities for regular vaccination against HS linked with FMD vaccination since simultaneous vaccination against both diseases has been shown to be effective.

1.4.2 Food and Agriculture Organization

During the last five decades of this century, the FAO has helped Sri Lanka, Thailand, Zambia and Myanmar to control HS. This assistance has included the services of consultants, training opportunities, equipment and supplies to strengthen national diagnostic and vaccine production laboratories. In Asia, a better focus on the assistance provided was made through the Animal Production and Health Commission for Asia and the Far East (APHCA) — a regional wing of the FAO, formed in 1973. Initially, the FAO sponsored two international meetings on HS, the first in Manila in 1959 and the second in Kuala Lumpur in 1962. The Manila meeting was attended by delegates from Burma (Myanmar), Ceylon (Sri Lanka), France, India, Iran, Iraq, Japan, Liberia, Malaya (Malaysia), Pakistan, Philippines, Thailand, United Kingdom, United States and Venezuela. The second meeting was equally well represented, with delegates from Australia, Burma, Ceylon, France, Republic of Guinea, India, Indonesia, Italy, Laos, Malaya, Philippines, Singapore, Sudan, Thailand and the United States. At these two early meetings on HS, a consensus was reached on a number of broad areas, including:
• that increased cooperation be established between research workers in different countries and that the coordination of research and investigational efforts directed towards control of the disease be strengthened;

• that facilities for training in specialised techniques be made available;

• that the diagnostic tests and vaccine production techniques be standardised;

• that due recognition be given to the need for combined vaccines and effective simultaneous vaccination against other diseases present in the region;

• that arrangements be made for collection and dissemination of information relating to the disease within the relevant countries.

It was also agreed that these objectives could be met by the following means:

• designate an institution in the Asian region as a reference centre for HS, and also examine the possibility of recognising such centres in other regions; and

• convene regular meetings on HS, to be held at the invitation of member countries.

After a decision was made by APHCA at its annual sessions in 1978, the third international meeting on HS was held in Colombo, Sri Lanka in December 1979. Prof. R.V.S. Bain was commissioned to visit all APHCA member countries, to assess the status of the disease and to submit a report, which formed the basis for the meeting. This meeting was attended by delegates from India, Indonesia, Iraq, Malaysia, Nepal, Sri Lanka and Thailand. Country reports were also submitted by Bangladesh and Pakistan.

The recommendations made at this meeting are summarised below.

• That the offer made by the Government of Sri Lanka to establish the regional reference centre in Sri Lanka be considered favourably by the FAO. A special subcommittee recommended that this centre should:

  • make available strains of known serotype and immunogenicity as vaccine seed;
  • provide a serotyping service for cultures associated with HS in particular and also other pasteurelloses;
  • provide national laboratories with reference cultures, reagents and vaccines;
  • provide training facilities in diagnostic procedures, including serotyping, vaccine production and testing.

• That further trials be carried out on the double emulsion vaccine, which has an improved syringeability.

• That the monograph on HS published by the FAO in 1963 (Bain 1963) be revised by a group of authors.

• That besides implementing the present knowledge on the disease, further research be encouraged on the following aspects:

  • carrier state of serotype 6:8 in cattle, buffalo, pigs, sheep, goats and poultry;
  • vaccine strain selection;
  • formulation of media for dense culture production for vaccines, using locally available ingredients; and
  • development and testing of vaccines based on newer microbiological concepts.

• That the APHCA secretariat serve as a centre for collection and dissemination of information.

• That in recognition of the usefulness of a uniform system of serotype designation, the capsular typing system of Carter and the somatic typing system of Namioka and Murata be adopted.

In pursuance of the recommendation of the third international meeting, the FAO designated the Veterinary Research Institute, Peradeniya, Sri Lanka as a regional reference centre for HS for the Asian region in 1985. The FAO provided some support to upgrade the facilities at this institute. A reference centre for the African region was in existence in Senegal in West Africa.
At the 1986 annual sessions of APHCA, a decision was made to set up an HS subgroup. This subgroup consisted of members from Indonesia, Malaysia, Sri Lanka and Thailand. The main task entrusted to the subgroup was to accelerate and coordinate the work aimed towards improving the quality of the vaccines. Two meetings of the subgroup were held in Bangkok, in September 1987 and February 1990. Priority areas for research and development on vaccines were identified as follows:

- the formulation of improved oil adjuvant vaccines with low viscosity and high stability without affecting potency;
- development of the double emulsion vaccine;
- development of vaccines based on the identification and characterisation of the protective antigens;
- development of live vaccines using strains which are avirulent or are of low virulence; and
- evaluation of all HS vaccines produced in the region at the regional reference centre.

These areas of vaccine research are described in more detail in Chapter 9. The fourth international meeting on HS was held in Kandy, Sri Lanka in February 1991 and was attended by delegates from India, Indonesia, Iran, Laos, Malaysia, Nepal, Philippines, Sri Lanka and Thailand. Additionally, with support received from the British Council and ACIAR, as well as APHCA, it was possible to obtain the participation of several resource personnel. These included two scientists from the United Kingdom, closely associated with the Moredun Research Institute, where considerable advances have been made on pasteurella vaccines, one from the CSIRO, Australia, and one from Japan.

The discussions at this meeting led to the identification of some important areas warranting further research and investigation:

- studies on pathogenesis of HS;
- investigations into the factors that determine virulence of the organism;
- comparison of serotyping systems and adoption of the most appropriate system;
- an evaluation of the usefulness of new laboratory techniques such as enzyme-linked immunosorbent assay (ELISA), polyacrylamide gel electrophoresis (PAGE), immunoblotting etc;
- determination of the criteria for declaration of disease-free status to a given area;
- studies on the carrier status of vaccinated animals;
- further confirmation as to whether naturally immune animals (also carriers) are resistant to challenge;
- investigations into thinner emulsions, and non-oil based adjuvants;
- studies on live vaccines and in vivo antigens.
- development of combined vaccines; and
- development of simplified methods for evaluation of vaccines.

In addition to supporting countries that needed assistance and organising scientific meetings, the FAO has produced a number of publications directly on HS or on a broader field including this disease:

1.4.3 Australian Centre for International Agricultural Research

ACIAR is a statutory authority established in Australia under an Act of Parliament. It has a mandate to facilitate collaborative research on high priority problems of developing countries that offers good prospects for mutual benefits with Australia. This is achieved by linking Australian research institutions with overseas research groups. In keeping with its mandate, ACIAR has maintained an interest in HS, which is a major animal health problem in the region. During the past decade, ACIAR has funded two projects specifically on HS, another dealing with a variety of diseases including HS, and another in the related field of pasteurellosis in pigs and poultry. A brief description of these projects is given below.

**Development of an improved haemorrhagic septicaemia vaccine**

This was a collaborative project between the CSIRO Division of Animal Health in Australia and the Veterinary Research Institute in Ipoh, Malaysia. This project broadly aimed at producing improved vaccines and developing and evaluating existing as well as newly developed tests for determining the efficacy of vaccines. Broadly two types of vaccines were developed. These were improved emulsion type vaccines which had low viscosity and easier injectability as well as vaccines based on the identification and characterisation of the cell components with a view to determining the protective antigens (see Chapter 7). Conventional tests such as the indirect haemagglutination test (IHA) and the passive mouse protection test (PMPT) were compared with a newly developed ELISA test and direct challenge.

**Diagnosis and control of haemorrhagic septicaemia in Indonesia**

This was a collaborative project between the Victorian Institute of Animal Science in Australia, the Research Institute for Veterinary Science in Bogor, Indonesia and the Disease Investigation Centre in Denpassar, Indonesia. This project covered a wide spectrum of areas connected with the diagnosis and control of HS.

- Improvement of techniques to detect the organism, including the development of special transport media and their evaluation in comparison with the conventional culture techniques.
- Development of molecular tests for detection of the organism as well as for characterisation with special emphasis on strain variation.
- Review of management and vaccination strategies.
- Retrospective and prospective studies of the sero-epidemiology of the disease, as well as sero-epidemiological studies using the ELISA test.

**Establishment of improved methods for the diagnosis and control of livestock diseases in Southeast Asia using ELISA**

This project was a collaboration between four institutions: the CSIRO Division of Animal Health and the Victorian Department of Agriculture and Rural Affairs in Australia; the Research Institute for Veterinary Science in Bogor, Indonesia; and University of Pertanian in Malaysia. Amongst other diseases, this project aimed at developing and evaluating the ELISA technique for identification of *Pasteurella multocida* strains causing HS as well as for detection of antibody against *P. multocida* in animals.

**Control of pasteurellosis in pigs and poultry**

This project had five participating institutions. These were Monash University and The University of Queensland in Australia; the Veterinary Research Institute in Peradeniya, Sri Lanka; and the National Institute of Veterinary Research and the National Veterinary Company in Vietnam. Though the project did not directly deal with bovine pasteurellosis, technologies developed may have future applications in the field of HS.
**International workshops**

ACIAR has also organised international meetings to enable scientists working on their research projects to present their findings. During the past decade, two such meetings sponsored by ACIAR were the International Workshop on Pasteurellosis in Production Animals, held in August 1992 (ACIAR 1993), and the International Workshop on Diagnosis and Control of Haemorrhagic Septicaemia in May 1996. Both workshops were held in Bali, Indonesia, with the participation of other scientists in the field as well. These workshops provided an excellent opportunity for those working in the field of HS in the region to exchange their views and share their experiences. Additionally, the participation of scientists from outside the region enabled the infusion of new ideas and technologies into this problem of utmost economic importance to the region.
Overview

History and nomenclature

Haemorrhagic septicaemia (HS) is caused by specific serotypes of the bacterium *Pasteurella*. The organism is named after Louis Pasteur in recognition of his pioneering work in the 1880s. The genus *Pasteurella* belongs to a large family of bacteria — the Pasteurellaceae, which includes two other important genera, *Actinobacillus* and *Haemophilus*. Two members of the genus *Pasteurella* — *P. multocida* and *P. haemolytica* — cause a variety of important diseases in domestic, agricultural and wild animals.

*Pasteurella multocida*

Several methods have been developed to identify different serotypes of *P. multocida*. These can be broadly grouped into methods that identify five 'capsular' antigens (based on components of the outer cell layer) and up to 16 'somatic' antigens (based on core components). Using a combination of capsular and somatic typing, the two common HS serotypes (popularly known as the Asian and African serotypes) are designated B:2 and E:2, respectively.

*Pasteurella haemolytica*

*P. haemolytica* can be distinguished from *P. multocida* by several biochemical characteristics. Two biotypes have been identified, based on sugar fermentation (A and T), while 16 types have been identified based on capsular polysaccharides.

2.1 History and Nomenclature

Haemorrhagic septicaemia (HS) is caused by specific serotypes of the bacterium *Pasteurella multocida* in cattle and buffaloes. According to current classification, the family Pasteurellaceae (Pohl 1981) includes a large group of gram-negative bacteria that are chemoorganotrophic, facultatively anaerobic and fermentative. The family has three genera: *Pasteurella* (Trevisan 1887), *Actinobacillus* (Brumpt 1910) and *Haemophilus* (Winslow et al. 1917). Several other species that exhibit complex phenotypic and genotypic relationships with these genera are also included. Most members of the family cause disease in mammals (including humans), birds and reptiles.

The first description of the bacterium was in 1878–79 when Rivolta and Revolee reported an outbreak of disease in fowl. About the same time, a disease in cattle and buffaloes was described by Bollinger in Germany. Its causative organism was isolated by Kitt in 1885. Gaffky described a septicaemic disease in rabbits in 1881 and Loeffler described a similar disease in swine in 1886. It was the German pathologist Hueppe who, in 1886, observed similarities in all of these diseases and also similarities in the bacteria associated with these disease conditions. Later, in 1887, Oreste and Armanti described a similar disease called 'barbone' in buffaloes in Italy, also caused by a similar organism; they proposed the name *Bacillus septicaemiae* for this bacterium. However, in 1887, Trevisan proposed the name *Pasteurella* to commemorate the work of Louis Pasteur on the aetiology of fowl cholera, which is caused by the same organism. Human infections caused by the same organism were described for the first time in 1920.

Since this bacterium caused disease in many species of animals, species names were initially given according to the host species in which it caused disease. Thus,